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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/568,332	02/13/2006	Gunter Stempfer	BP/G-33315A/BCK	6279
72554	7590	05/01/2009		
SANDOZ INC 506 CARNEFIE CENTER PRINCETON, NJ 08540			EXAMINER WEGERT, SANDRA L	
			ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/568,332	Applicant(s) STEMPFER ET AL.	
	Examiner SANDRA WEGERT	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 January 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 13-24 is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The amendment and Remarks, sent 21 January 2009, have been entered into the record.

Claims 1, 2 and 20 have been amended. Claim 24 is new and reads on the elected invention.

Claims 1-24 are under examination in the Instant Application.

Withdrawn Objections and Rejections

Claim Objections-

The objection to claim 13 and dependent claims 14-23, for failing to provide proper antecedent basis for the claimed subject matter, is *withdrawn*. Applicants pointed to p. 5 of the instant Specification where the method steps are recited in the same order as found in the claims (21 January 2009, Remarks, p. 5).

Claim Rejections- 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Art Unit: 1647

The rejection of claims 20 and 21, under 35 U.S.C. 112, second paragraph, for being indefinite is *withdrawn*. Independent claim 20 previously did not have sufficient antecedent basis for the limitation "said prokaryotic host" (see Office Action, 18 August 2008, p.4).

Applicants amended claim 20 by having it now depend from claim 24, from which it does derive proper antecedence (21 January 2009).

Claim Rejections- 35 USC § 102

The following is a quotation of the appropriate paragraph of 35 U.S.C. 102 that forms the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The rejection of claims 1-12 under 35 U.S.C. 102(e) for being anticipated by Kwon et al (US 2004/0151695 A1) is *withdrawn*. Kwon et al disclose a method for producing human interferon alpha, including human interferon alpha 2A (as required by claims 10-12), by recombinantly expressing and secreting human interferon by a genetically modified *E. coli* (see paragraph 33, Fig. 5a and 5b and Examples 1-3). The fermentation steps are prior to the step of resuspension of the collected bacterial cells in distilled water at 4 °C to extract proteins by

Art Unit: 1647

osmotic shock. Thus, as argued by applicants (Remarks, p. 8), the cells were not disrupted *within* the fermentation medium, as required by the amended independent claim.

Maintained/New Claim Rejections/Objections

Claim Objections-

Claims 11 and 12 are objected to for depending from a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112- second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 7-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rendered indefinite for use of the word "agent" in the phrase: *adding an agent directly to the fermentation medium*. It is not clear what is meant by agent in this case, as it is not defined or limited in the newly-added phrase.

Claims 7-12 are included in this rejection because they are ultimately dependent from the specifically-mentioned claims without resolving the indefiniteness issue belonging thereto.

Claim Rejections- 35 USC § 102

The following is a quotation of the appropriate paragraph of 35 U.S.C. 102 that forms the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-10 under 35 U.S.C. 102(b) as being anticipated by Bochner et al (1987, US Patent 4,680,262) is *maintained*. Bochner et al disclose a method for the preparation of growth hormone or any peptide of interest from transformed E. coli cells. The reference describes the process of fermentation as culturing the cells at 37 °C and pH 7.5 for 36 hours, after which steam is immediately injected into the fermenter jacket, the temperature of the tank rises rapidly to 50 °C, and the high temperature is held for 10 minutes (Example 8, column 12). The polypeptides are described as being injected into the *periplasm* of the transformed E. coli host cells (see Title and Abstract) as recited by the instant independent claims. In addition, the reference discusses extraction of the polypeptide of interest by osmotic *shock* (column 2, line 46), as recited in claims 1 and 2 and encompassed by all claims. In addition, Bochner et al discuss agents used for osmotic shock, such as *sucrose* (column 5, line 32), as well as typical concentrations used, such as *20% sucrose*, as recited in claims 3-6. Terms specific to Claims 7-10 are disclosed throughout the reference: the bacteria are *Gram-negative* (Column 1, line 48);

Art Unit: 1647

the host cell used was *E. coli* (see Example 1); and the reference discloses a method of producing *other polypeptides of interest* (column 1, paragraph 4), as required by claim 10.

Applicants have argued against Bochner, et al being used as prior art because they contend that Bochner, et al did not apply the osmotic shock to the cells *in the fermentation medium* as required by newly-amended independent claim 1 (Remarks, 21 January 2009, p. 5).

Applicant's arguments have been fully considered but they are not persuasive for the following reasons:

Bochner et al (1987, US Patent 4,680,262) *does* contemplate applying osmotic shock directly to the fermentation medium (see column 2, line 45; column 3, second paragraph and column 4, lines 56-58). The fact that Bochner, et al discusses both the advantages and disadvantages of immediate osmotic shock when cells have reached maximum growth (compare column 2 and column 4), does not subtract from the fact that they had contemplated and used just such a technique to potentially maximize protein production from the fermentation medium.

35 USC § 112, first paragraph - Written Description.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 7-12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

Art Unit: 1647

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 7-12 are directed to a process for the preparation of a recombinant polypeptide using fermentation methods with prokaryotic host cells, and extraction of the polypeptides by adding an "agent" directly to the fermentation medium. However, the claims do not specify precisely what substances may be used as "agents," nor do they even describe the properties that such an "agent" would possess, such that one could recognize whether applicants were in possession of such an agent or class of agents.

The specification teaches adding distilled water, sucrose, or alcohol to disrupt the prokaryotic bacteria in the fermentation medium. However, the specification does not teach functional or structural characteristics of an "agent," other than those listed, to be used for the claimed methods. The description of one or a few agents is not adequate written description of an entire genus of functionally-equivalent molecules that might include many other types of molecules or formulations.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a recitation of one functional requirements of the "agent," and one that has not been adequately identified. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*” (See page 1117). The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed” (See *Vas-Cath* at page 1116).

With the exception of the "agent" referred to above, the skilled artisan cannot envision the detailed chemical structure of the encompassed "agents" and, therefore, would not know how to use them. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of use. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of use. The agent *itself* is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, use of only a Db-specific monoclonal antibody, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Art Unit: 1647

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion:

Claims 1-12 are rejected for the reasons cited above. Claims 13-24 are allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Manjunath Rao, can be reached at (571) 272-0939.

Art Unit: 1647

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

/SLW/

23 April 2009

/Dong Jiang/
Primary Examiner, Art Unit 1646